

REMARKS

This Application has been carefully reviewed in light of the Office Action mailed November 18, 2004. At the time of the Office Action, Claims 1-18 and 25-32 were pending in this Application. Claims 19-24 and 33-79 were previously cancelled due to an election/restriction requirement. Claims 1-18 and 25-32 were rejected. Claims 1, 4, 6-7, 9-11, 13-15, and 29 have been amended to further define various features of Applicants' invention. Claims 2-3, 25-28, and 30-31 have been cancelled. However, Applicants reserve the right to request examination of non-elected species in Claims 2-3 and 30-31 should a generic claim be found allowable. Applicants have added new claims 80-141. No new matter is presented by these amendments. Applicants respectfully request reconsideration and favorable action in this case.

PTO-892 Cited References

Applicants would like to bring to the Examiner's attention that a copy of article entitled "*The AR04 gene of Candida albicans encodes a tyrosine-sensitive DAHP sythase: evolution, functional conservation and phenotype of Aro3p-, Aro4p-deficient mutants*" by Silvino Sousa et al. ("Sousa et al"), Microbiology (2002), 148, pp 1291-1303, was with the Office Action mailed November 18, 2004, however, the reference was not cited by the Examiner on the PTO-892. Applicants have included the reference in an Information Disclosure Statement submitted with this Response.

Claim Objections

Claims 2-3, 26-27, and 30-31 were objected to because they are partially drawn to non-elected inventions, and Claims 6, 9, 10, 13, 25, and 29 were objected to due to informalities. Applicants have cancelled Claims 2-3 and 30-31 and amended Claims 1 and 29 to recite only elected species.

Applicants have amended Claims 6, 9, 10 and 13 to recite the full version of terms used therein, rather than abbreviations to overcome the Examiner's objections. Claim 25 has

been cancelled and Claim 29 has been amended to no longer recite the previously abbreviated subject matter.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-18 and 25-32 were rejected by the Examiner under 35 U.S.C. §112, second paragraph, as being indefinite and failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner made several rejections based generally upon the use of the term “sequence” to refer to a physical entity. Applicants have now amended Claims 1, 10, 14, 15 and 29 to refer to a nucleic acid or polynucleotide having a particular sequence or encoding a protein having a particular amino acid sequence. All relevant newly added claims contain similar usages of the term “sequence.” Applicants submit that these amendments clearly indicate which physical entities have the specific sequences.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1-18 and 25-32 were rejected by the Examiner under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement and the enablement requirement. Applicants amend Claims 1 and 29 to recite a specific geranylgeranyl pyrophosphate synthase as well as a specific diterpene synthase. These specific synthases are described in detail in the specification, with full disclosure of their structures and methods of use. Thus, there is adequate written description of these nucleic acids, polynucleotides, and synthase proteins.

Regarding the Examiner’s comments on enablement of an organism comprising the polynucleotide of SEQ ID NO: 1 and the polynucleotide of SEQ ID NO: 361, Applicants submit that one skilled in the art would readily know how to make and use such an organism in light of the present application.

Methods for placing two different polynucleotides in an organism and using them to produce two different proteins have been known for some time. Some such methods, such as incorporation of the polynucleotides or nucleic acids on a vector taken up by the organism are described in the specification, although other methods are known in the art or may be

developed in the future. Selection of an appropriate method for a given outcome, such as long-term or short-term expression, or the type of organism, such as yeast, bacteria, insect, plant or mammalian cells is routine in the art. Given the demonstrated ability to insert nucleic acids or polynucleotides having SEQ ID NO:1 and SEQ ID NO:365 into an organism to produce a diterpene, there is no reason to believe that insertion of nucleic acids or polynucleotides encoding the other indicated geranylgeranyl pyrophosphate synthases and diterpene synthases, particularly the combination of those having SEQ ID NO:1 and SEQ ID NO: 361 would involve anything other than routine experimentation.

Additionally, Applicants believe that the Richmond reference cited by the Examiner merely further proves Applicants' point. Although the presence of an additional protein is not required by all embodiments of Claim 1, the copalyl diphosphate synthase of the Richmond reference is certainly not excluded. Accordingly, the Richmond reference merely shows that one skilled in the art would be able to readily determine what, if any, other proteins might be present in the organism to influence diterpene production. Addition of such a protein would be as simple a matter as the addition of any other protein. Applicants claim, through use of the term "comprising" specifically allows for the inclusion of other proteins or materials in the organism, so long as it is able to produce a diterpene.

Applicants are not required to perform an experiment to show that every possible combination functions, Applicants must merely provide experiments sufficient to establish a reasonable basis that use of any other claimed nucleic acid, polynucleotides, or proteins not explicitly included in the experiments would function without undue experimentation. MPEP 2164.02

Applicants have amended Claim 14 to recite a particular nucleic acid having a specific sequence. In new Claim 80, Applicants similarly recite a nucleic acid encoding a particular protein. The structure and function of this nucleic acid and protein are discussed, *inter alia*, at paragraph 98 of the Specification. Thus, adequate written description is provided. The Examiner does not appear to have asserted that any enablement for the recited nucleic acid or polypeptide was lacking.

Finally, Applicants assert that the genus of soluble HMG-Co-A reductases is described sufficiently in the specification to fulfill the written description requirement. The

inclusion of unknown members of a genus is in no way prohibited by §112. Merely a representative number of species need be disclosed, not every specific species encompassed by the genus. MPEP 2163(a)(ii). In the present application, Applicants have, in fact called out particular structural features significant for HMG-Co-A reductase as used in the invention near the end of paragraph 94. In particular, the sequences related to intracellular solubility and reductase activity are noted. Although not spelled out entirely in the Specification, such sequences are readily known in the art. Additionally, Claim 10 recites a soluble form of HMG-Co-A reductase, which is further described in paragraphs 92-95. Paragraph 84 provides the amino acid sequence for nearly 200 different soluble HMG-Co-A reductases. Given this very large number of specific examples as well as the structural guidelines in paragraphs 92-95, one skilled in the art would have no trouble identifying relevant structural features even of unknown HMG-Co-A reductases. Accordingly, adequate written description is provided for the genus.

Additionally, as explained above, Applicants are by no means required to provide actual experimental data for every possible claimed combination of the invention. Applicants have shown that the hmg 1 p yeast HMG-Co-A reductase gene may be inserted into an organism with a geranylgeranyl pyrophosphate synthase and a diterpene synthase to produce a diterpene. Insertion of other HMG-Co-A reductases involves only routine experimentation and is thus enabled.

Information Disclosure Statement

Applicants enclose an Information Disclosure Statement and PTO Form 1449, with a copy of the reference and a check in the amount of \$180.00, for the Examiner's review and consideration.

CONCLUSION

Applicants have now made an earnest effort to place this case in condition for allowance in light of the amendments and remarks set forth above. Applicants respectfully request reconsideration of Claims 1, 4-18, 29, 32, and 80-141 as amended.

Applicants enclose a Petition for Extension of Time. Applicants believe a fee of \$225 is due under 37 C.F.R. 1.17(a)(2) for a two month extension of time in connection with this response. A check in that amount is provided. Applicants believe there are no additional fees due, however, the Commissioner is hereby authorized to charge any additional fees or credit any overpayment to Deposit Account No. 50-2148 of Baker Botts L.L.P. in order to effectuate this filing.

If there are any matters concerning this Application that may be cleared up in a telephone conversation, please contact Applicants' attorney at 512.322.2580.

Respectfully submitted,
BAKER BOTTS L.L.P.
Attorney for Applicants



Michelle M. LeCointe
Reg. No. 46,861

SEND CORRESPONDENCE TO:
BAKER BOTTS L.L.P.
CUSTOMER ACCOUNT NO. **31625**
512.322.2580
512.322.8380 (fax)

Date: 4/18/05